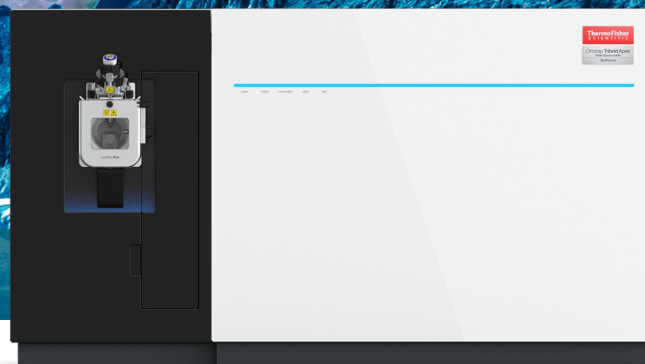




Mass spectrometry



Rise to the molecular challenges of today and tomorrow

Orbitrap Tribrid Apex BioPharma mass spectrometer

Benefits

- Preserves native protein aggregates with enhanced ion decluttering via IR-laser desolvation
- Single-platform versatility for intact biologics, peptide mapping, and small molecules
- Increased sequence coverage of large biopharmaceuticals using advanced fragmentation, including IR-laser
- Accurate oligonucleotide sequencing up to 100-mer with low-q CID
- Deeper insight into molecular heterogeneity using Direct Mass Technology or PTCL

Be prepared for the world ahead with our most flexible instrumentation—Thermo Scientific™ Orbitrap™ Tribrid™ Apex BioPharma Mass Spectrometers. Enjoy ultimate flexibility while maintaining ease of use with proven technology. Characterize the largest biopharmaceuticals from native fusion proteins to oligonucleotides, all the way down to the smallest pharma molecules with optional alternate fragmentation and ion manipulation techniques. We're introducing a new commercial IR-laser for more efficient ETD fragmentation, better ion desolvation for native analyses of large molecules, and improved generation of Thermo Scientific™ TMT™ reporter ions, delivering yet another innovative solution for real experimental problems.

Reach new peaks with the advanced accuracy, accessibility, and adaptability of the Orbitrap Tribrid Apex BioPharma mass spectrometer.

Key capabilities

- Unique Thermo Scientific™ Tribrid™ architecture includes a quadrupole mass filter, a dual-pressure linear ion trap, and Thermo Scientific™ Orbitrap™ mass analyzers, allowing unique combinations of high-sensitivity IT analyses, high-resolution OT analyses, and a broad range of MSⁿ acquisition types using a variety of fragmentation and manipulation techniques
- High-sensitivity atmospheric pressure interface combines a high-capacity transfer tube (HCTT) and a robust electrodynamic ion funnel (EDIF), providing a high ion flux and low limits of detection for a wider range of molecules
- Active Ion Management (AIM+) technology, which includes the QR5 segmented quadrupole mass filter with hyperbolic surfaces, maximizes ion transmission to achieve unprecedented levels of qualitative and quantitative performance
- Dual Ion Routing Multipoles (IRMs) maximize instrument duty cycle and ion utilization during even the most complex MSⁿ acquisitions
- Improved parallelization of MS and MSⁿ analyses with new maximum injection times, providing extra sensitivity without compromising acquisition rates
- Automated, remote, and hands-free calibration with the Thermo Scientific™ Auto-Ready 2 ion source, allowing the user to spend more time obtaining results and less time on instrument setup
- Optional Native MS mode provides expanded MSⁿ mass range capabilities for comprehensive characterization of proteins and protein complexes
- Expanded quadrupole isolation range with Native MS option for higher sensitivity precursor selection at high *m/z*, advancing native structural analysis
- Real-time search of a database or a spectral library enables faster data acquisitions and improved specificity, significantly increasing analytical performance, including TMT-based quantification experiments
- Thermo Scientific™ TurboTMT mode improves HRAM MSⁿ acquisition rates in TMT experiments
- Thermo Scientific™ Precursor Fit filter enables precursor ion selection for a defined specificity
- New ion optic enhances vacuum and improves Orbitrap mass analyzer performance
- Environmentally friendly, oil-free dry pumps are standard for less maintenance and leak-free vacuum performance
- DDA and DIA MS/MS acquisition rates of up to 75 Hz with 3,750 resolving power at *m/z* 200 for the Orbitrap mass analyzer and 100 Hz under select linear ion trap scan conditions and injection times
- New Orbitrap resolutions from 1,875 up to 480,000 FWHM at *m/z* 200, depending on acquisition mode
- Improved linear ion trap electron multiplier detector with significantly longer lifetime and robustness
- Synchronous Precursor Selection (SPS) for MSⁿ experiments
- Optional laser ion activation—choose between a UV- or IR-laser source to support application-specific orthogonal ion activation
- Recommended compact Electron Transfer Dissociation (ETD) and optional Proton Transfer Charge Reduction (PTCR) ion source based on Townsend discharge with extremely stable anion flux for improved usability and reagent longevity
- Multiple fragmentation techniques are available at any MSⁿ stage, with detection in the Orbitrap or the linear ion trap mass analyzers
 - » Resonant collision-induced dissociation (CID) and higher-energy collisional dissociation (HCD)
 - » Optional ETD, including electron-transfer higher-energy collision dissociation (ET_hcD) and electron-transfer collision-induced dissociation (ET_ciD)
 - » Optional laser activation with ultraviolet photodissociation (UVPD) or infrared multiphoton dissociation (IRMPD) and IR ion activation for ETD
- New IR-desolvation gently removes solvent/detergent from large protein complexes while preserving native structure
- Optional PTCR simplifies MSⁿ spectra of multiply charged analytes
- New optional Direct Mass Technology mode enhances sensitivity across all MSⁿ levels, supports any alternative ion activation, and is easy to use—making it ideal for complex samples
- Advanced Peak Determination (APD) for improved precursor annotation in data-dependent experiments
- Smart targeted TMT workflow powered by Adaptive real-time library search (RTL_S) for sensitive and precise quantification

- Intuitive, flexible drag-and-drop instrument method editor simplifies method development and creation of unique analytical workflows
- Extensive pre-built and optimized method templates are fully customizable for a variety of application workflows
- Thermo Scientific™ AcquireX™ data acquisition workflow provides all-inclusive, automated small-molecule sample profiling on an LC timescale
- Streamlined calibration routines with improved Orbitrap calibration for ions with $m/z < 200$

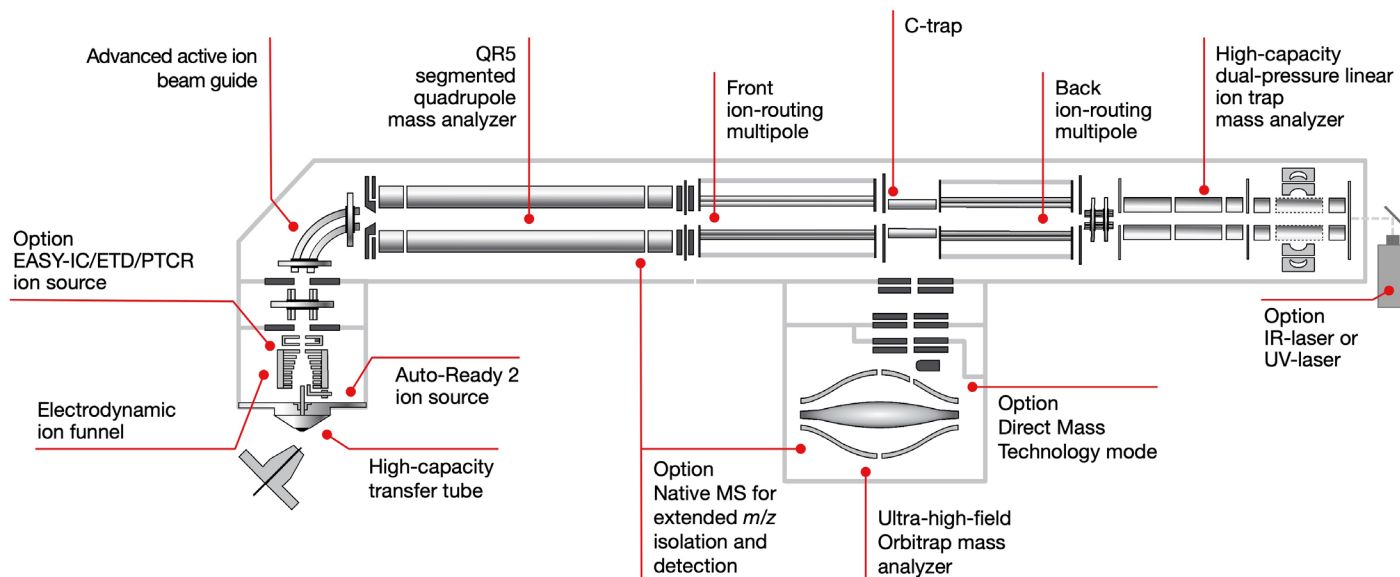


Figure 1. Orbitrap Tribrid Apex BioPharma mass spectrometer ion path.

Hardware features

Active Ion Management (AIM+) technology

AIM+ maximizes ion transmission, from injection to detection, using a hardware design for precise management of electrical fields and removal of noise to achieve unprecedented levels of quantitative performance.

Ion source

Thermo Scientific™ OptaMax™ Plus ion source

- Enhanced stability—the new heater and sprayer design significantly enhances heat transfer, offering superior electrospray stability across a broad temperature range
- User-friendly design—experience enhanced ease of use with adjustable and reproducible movement, simplifying your workflow
- Versatile flow rate compatibility—supports a wide range of flow rates from 1–2,000 $\mu\text{L}/\text{min}$, providing flexibility for various applications

- Optional Atmospheric Pressure Chemical Ionization (APCI) probe—the optional APCI probe is compatible with flow rates from 100–2,000 $\mu\text{L}/\text{min}$ and can be upgraded with Atmospheric Pressure Photoionization (APPI) capabilities for expanded functionality

Auto-Ready 2 ion source

- Integrated source with dedicated emitter and ion transfer tube simplifies maintenance and calibration
- System checks and calibrations can be triggered on demand or scheduled without disruption to your LC-MS configuration
- Calibration and maintenance results are controlled and reported directly in the instrument control software interface
- Internal Thermo Scientific™ Pierce™ FlexMix™ Calibration Solution consumable lasts ≥ 3 months with weekly mass calibration and monthly system calibration, plus intermittent checks

New generation ion optics and mass analyzers

Optional ETD, EThcD, ETciD, IRMPD, IR-ETD, IR-EThcD, IR-ETciD, and UVPD.

High-capacity transfer tube

- The HCTT increases ion flux into the vacuum system for improved sensitivity
- Offers vent-free maintenance

Electrodynamic ion funnel

- A robust ion funnel captures the ions under more gentle conditions, improving the transfer of labile compounds while maintaining optimal transmission
- Automatic tuning results in broad ion transmission curves with reduced ion losses, increasing sensitivity

Advanced active ion beam guide (AABG)

AABG with an axial field and low-pass filter prevents neutrals and high-velocity clusters from entering the quadrupole mass filter.

QR5 segmented quadrupole mass filter with hyperbolic surfaces

Quadrupole mass filter with 5.25 mm field radius delivers industry-leading ion transmission across m/z 50–2,000 range for efficient precursor selection with m/z 0.4–3,000 isolation width.

Front ion-routing multipole

- Ion storage capabilities
- HCD on MS²
- Variable pressure control from 0.5–20 mTorr with Native MS option for small- and large-molecule workflows
- Efficient and reliable ion transfer between the ion-routing multipole, Orbitrap mass analyzer, and linear ion trap mass analyzer

Orbitrap mass analyzer

- Ultra-high-field Orbitrap mass analyzer
- Low noise detection pre-amplifier
- Automatic calibration of all ion transfer parameters

Dual-pressure linear ion trap mass analyzer

- MSⁿ, $n = 1$ through 10, using any available fragmentation technique
- Extended front section of the high-pressure cell for improved ETD and PTCR reaction control
- Precursor isolation width range from 0.2–4,000 m/z for precursors from 50–4,000 m/z for normal mass range isolations
- m/z mass range from 50 to 4,000
- CID, ETD/EThcD/ETciD, IRMPD, and UVPD fragmentation techniques
- PTCR ion-ion reaction
- IR-desolvation of large and complex ions
- Low-pressure cell for improved scan rates, resolving power, and mass accuracy
- Dual-dynode detector with high linear dynamic range for improved quantification and increased lifetime and robustness

Vacuum system

- Multiple turbomolecular pumps create vacuum stages ranging from >1 Torr down to $\sim 1 \times 10^{-10}$ Torr
- Stainless steel and aluminum high-vacuum analyzer chambers
- Enhanced vacuum technology reduces the pressure in the ultra-high vacuum region to $<10^{-10}$ Torr
- Improved Orbitrap mass analyzer performance at a wider range of collision gas settings
- Improved vacuum management and UHV pump design for optimal UHV pressures and noise characteristics

Analog inputs

- Channel 1 analog input (0–10 V); channel 2 analog (0–2 V)

Optional hardware and software

Thermo Scientific™ EASY-IC™ ion source (recommended)

- Generates internal calibrant ions for real-time mass calibration of spectra in positive and negative modes
- Provides <1 ppm RMS drift over 24 hours, measured with Pierce FlexMix calibration solution

Thermo Scientific™ EASY-ETD™ ion source (recommended)

- Generates fluoranthene anions for ETD
- Townsend discharge provides extremely stable and robust fluoranthene ionization
- Compact size, located entirely within the footprint of the instrument
- Active reagent ion filtering using the quadrupole mass filter
- Optimized charge-state-dependent calibration of reaction time to maximize spectral quality
- Improved dynamic range and signal-to-noise ratio (S/N) for fragments using high-dynamic-range EASY-ETD HD
- Faster reaction times for improved duty cycles

Thermo Scientific™ PTCR ion source (recommended)

- Extension of the EASY-ETD ion source
- Generates perfluoroperhydrophenanthrene (PFPP) ions for subsequent gas-phase charge reduction by ion-ion reactions
- Simplifies interpretation of complex spectra by decreasing the charge state of precursors and/or product ions at the MSⁿ level

Thermo Scientific™ IR-laser source (recommended)

- Class 1 laser MS system incorporating a Class 4, 10.6 μm wavelength Coherent™ CO₂ laser system with 30 W continuous wave output
- Specialized operation mode to enhance TMT reporter ion generation
- Enables supplemental IR activation during ETD to improve the formation of c/z fragment ions
- Performs ion desolvation before MS¹ analysis or subsequent MSⁿ stages
- Enables precursor dissociation with IRMPD at any MSⁿ stage, with detection in either the ion trap or Orbitrap analyzer

Thermo Scientific™ UV-laser source

- Class 1 laser MS system incorporating a Class 4, 213 nm wavelength CryLaS™ laser system with 2.5 kHz repetition rate, delivering >1.2 μJ per pulse
- Performs dissociation of precursors at any stage of MSⁿ, with detection in either the ion trap or Orbitrap mass analyzer
- Compact size, located entirely within the footprint of the instrument

Direct Mass Technology mode (recommended)

- Charge detection for the simultaneous measurement of m/z and z
- Measures hundreds of individual ions in parallel
- Up to 10-fold increase in resolution relative to traditional ensemble ion measurements
- Requires less sample or less concentrated samples
- Automatic Ion Control (AIC) maintains single ion per m/z conditions in every spectrum

Native MS option (recommended)

- Extends the MS¹ mass range to m/z 16,000 for detection of large precursors and up to m/z 20,000 for MSⁿ ($n>1$) product ions in the Orbitrap mass analyzer
- Extends the ion isolation range in the quadrupole to include m/z 2,000 to 12,000, with m/z 5–3,000 isolation width
- Extends the ion isolation range up to m/z 8,000 in the ion trap with isolation widths $>m/z$ 100

Thermo Scientific™ FAIMS Pro Duo interface (optional)

- Performs online gas-phase fractionation based on differential ion mobility
- Optimized performance for 100 nL/min to 1 mL/min flow rates

OptiSpray technology

- Maximum low-flow electrospray ionization performance and reproducibility using automated spray optimization with integrated sheath gas control
- Simple installation, use and usage tracking of cartridge nano and capillary columns
- Enhanced robustness with exchangeable emitters and inactive spray position between injections
- Supports Thermo Scientific™ OptiSpray™ cartridge columns
- Compatible with flow rates from 50–10,000 nL/min

Thermo Scientific™ NanoSpray Flex NG™ ion source

- Supports static and dynamic electrospray experiments
- Compatible with liquid flow rates of 50 nL/min–2 μL/min

Thermo Scientific™ EASY-Spray™ ion source

- Maximum nanoelectrospray performance with no need for adjustments

Software features

Data system

- High-performance PC with Intel™ microprocessor
- High-resolution LED color monitor
- Microsoft™ Windows™ 11 operating system

Thermo Scientific™ Xcalibur™ software

- Xcalibur software is the control software for the next-generation Thermo Scientific™ mass spectrometer portfolio
- Accelerates familiarization and reduces training needs

Orbitrap Tribrid Apex MS instrument control software

- Tune application for instrument calibrations and check diagnostics and manual data acquisition
- Method editor with a comprehensive application-specific template library, method setup supported by tooltips, and a drag-and-drop user interface to facilitate method development

Optional data analysis software

Thermo Scientific™ Proteome Discoverer™ software

Flexible, expandable platform for the qualitative and quantitative analysis of proteomics data.

Thermo Scientific™ ProSightPD™ software

Processing node within Proteome Discoverer software that allows execution of ProSight searches of top-down and middle-down data.

Thermo Scientific™ BioPharma Finder™ software

Integrated solution for protein-based biotherapeutic analysis through molecular and sub-structural data processing, utilizing deconvolution and predictive fragmentation pattern algorithms.

Thermo Scientific™ Compound Discoverer™ software

Platform for small-molecule structural identification and comparative data analysis.

Operation modes

Top speed

Maximizes the number of high-quality MSⁿ spectra in each cycle by intelligently scheduling MS and data-dependent MSⁿ scans based on a user-defined time between adjacent survey spectra.

TopN

Enables a user-defined maximum number of high-quality MSⁿ spectra from each cycle.

Dynamic maximum injection time

Maximizes the amount of high-quality data acquired by synchronizing operations of ion injection, ion transfers within the instrument, and operation of the linear ion trap and Orbitrap mass analyzers.

Advanced peak determination

Precursor annotation algorithm for improved charge-state assignment to increase the number of precursors available for data-dependent analysis.

Exclusive technologies

Dynamic scan management

Enables intelligent, real-time scheduling, parallelization, and prioritization of acquisition events, and selection, sorting, and routing of precursors to different fragmentation modes and analyzers based on user-selected parameters, including precursor *m/z*, intensity, and/or charge.

Multiple dissociation options

Precursor dissociation can be performed in the ion-routing multipoles (HCD), the linear ion trap (CID, ETD/ETciD, or optional UV-laser and optional IR-laser), or both (EThcD), with product ion detection in the linear ion trap or Orbitrap mass analyzer at any stage of MSⁿ analysis.

Automatic gain control

Helps ensure that the ion-routing multipole is always filled with the optimum number of ions for any acquisition type.

Proton transfer charge reduction option

Performs ion-ion reaction to reduce charge states of selected precursors or product ions, and can be applied at any stage of MSⁿ analysis.

Real-time database search

Searches user-defined database in real time to then select identified/or not-identified precursors for further MSⁿ experimentation. Example: Selection of identified precursors only for SPS MS³ quantitation increases the accuracy and proteome coverage of TMT experiments.

Dual mass range quadrupole isolation

Optimal isolation performance at toggled low and high *m/z* range, using enhanced, novel dual residence RF capabilities.

Real-time library search

Intelligent acquisition provides higher confidence with real-time spectral matching against a local, customizable spectral library for decision-based triggering of MSⁿ acquisition events. It enables library-directed MSⁿ data acquisition to increase confidence in annotation, including structurally related compounds, and improve structured assignment of isomeric species, unknown characterization, and other applications.

Adaptive RT routine

The method leverages a novel real-time mapping routine to dynamically adjust timed/scheduled data acquisition windows to narrower time intervals and boost data acquisition performance by eliminating missing values that compromise data quality.

TurboTMT mode

Novel processing mode powered by Phase-Constrained Spectrum Deconvolution Method (ϕSDM) designed to improve the acquisition rate of TMT experiments.

Precursor Fit filter

Allows selection of precursors with defined specificity.

Advanced data-dependent experiments

TMT SPS MS³ aided by real-time search

TMT SPS MS³ experiment with real-time protein database search to perform SPS MS³ only on identified precursors.

Smart targeted TMT workflow

A real-time analytics workflow that enables next-generation TMT-based multiplexed targeted proteomics. Adaptive RTLS will perform real-time elution monitoring and MS² spectral matching to identify targets and prompt SPS-MS³ acquisitions to quantify hundreds of targets with robustness and sensitivity.

Universal method

Powered by Dynamic Maximum Injection Time, helps ensure the best results from samples with unknown concentrations.

Product-ion-triggered MSⁿ

Fragment-ion- or neutral-loss-triggered MSⁿ experiment, including at the same MSⁿ level.

Isolation offset

Custom centering of the precursor isolation window, optimized for broad isotopic distributions.

Thermo Scientific™ SureQuant™ internal standard (IS) targeted protein quantitation workflow

Enhanced PRM experiment that leverages internal standards to guide and automatically maximize outcomes and data quality for real-time targeted proteomics analysis.

Performance specifications

Orbitrap mass range	m/z 40–6,000 experiment and mode (dependent on mass range and MS ⁿ order)
Orbitrap resolution	Resolution settings range from 1,875–480,000 (FWHM) at m/z 200, with isotopic fidelity up to 240,000 FWHM
Acquisition rate*	Orbitrap MS/MS acquisition rates up to 75 Hz when measured using a data-dependent experiment or data-independent with Pierce FlexMix calibration solution, MS and HCD MS/MS resolution setting of 3,750 at m/z 200, with a maximum ion fill time of 8 ms. Linear ion trap MS/MS acquisition rates up to 100 Hz using Pierce FlexMix calibration solution and HCD MS/MS ion trap detection m/z range less than 200, with an MS/MS maximum ion fill time of <5 ms.
Orbitrap mass accuracy*	External calibration achieves <3 ppm RMS drift over 24 hours, measured with Pierce FlexMix; internal calibration achieves <1 ppm RMS drift over 24 hours, measured with Pierce FlexMix
MS/MS Electrospray Ionization (ESI) ion trap sensitivity	2 μ L of a 50 fg/ μ L solution of reserpine (100 fg total) injected at a flow rate of 500 μ L/min produces a minimum S/N of 200:1 for the transition of the isolated protonated molecular ions at m/z 609 to the largest two product ions, m/z 397 and m/z 448, when the mass spectrometer is operated at unit resolution in the full scan MS/MS mode, m/z 165–615; the test requires the HESI II probe
Dynamic range	>5,000 within a single Orbitrap mass spectrum
MS scan power	Collects MS ⁿ , for $n = 1$ through 10, detected in the ion trap mass analyzer
Synchronous precursor isolation	Samples up to 20 precursors per MS ⁿ scan
Precursor multiplexing	Up to 20 precursors can be multiplexed using the quadrupole mass filter and front ion-routing multipole to perform selected ion monitoring or tandem MS
Quadrupole isolation range	Standard quadrupole with 5.25 mm field radius isolates from m/z 50–2,000 with isolation width of m/z 0.4–3,000
Polarity switching	One full experimental cycle acquired in <0.77 seconds equals >1.3 Hz, where the cycle consists of acquiring one full MS scan in positive and negative polarity at a resolving power setting of 60,000, running Pierce FlexMix with an average injection time of 2 ms

Optional performance specifications

ETD option efficiency	Reaction with ETD anions dissociates the isolated 2+ MRFA precursor (m/z 262) to generate a series of fragments that have a summed relative abundance $\geq 15\%$ to the precursor measured in the linear ion trap, using Pierce FlexMix calibration solution infused at 6 μ L/min
PTCR option efficiency	Reaction time of 100 ms causes isolated MRFA 2+ molecular ion (m/z 262) to convert to a charged reduced ion at m/z 524, with a relative abundance of $\geq 25\%$ to the precursor measured in the linear ion trap, using Pierce FlexMix calibration solution infused at 6 μ L/min
UV-laser option efficiency	Exposure of 100 ms dissociates the isolated caffeine molecular ion (m/z 195) to generate the m/z 138 product ion with a relative abundance of $\geq 25\%$ to the precursor measured in the linear ion trap, using Pierce FlexMix calibration solution infused at 6 μ L/min
IR-laser option efficiency	Exposure to 25% NLP at $q = 0.25$ causes isolated MRFA 2+ molecular ion (m/z 262) to generate a series of fragments that have a summed relative abundance >50% to the precursor when measured in the linear ion trap with a scan range of 110–600 m/z using Pierce FlexMix calibration solution infused at 6 μ L/min
Native MS option	Native MS mass detection range m/z 500–16,000 for MS ¹ and m/z 500–20,000 for MS ⁿ ($n > 1$) in the Orbitrap mass analyzer. Quadrupole isolation range to m/z 2,000–12,000 with isolation width range of m/z 5–3,000. Ion trap isolation range up to m/z 8,000 with isolation widths > m/z 100.
Direct Mass Technology mode	With low-pressure settings and an m/z range of 600–2,000, more than 50% of myoglobin 20+ ions (m/z 848) will have lifetimes >1.0 seconds when processed with STORlboard software under specific conditions

*Under defined conditions

Installation requirements

Power

- 230 V AC $\pm 10\%$ single-phase, 50/60 Hz, with ground, 2 outlets at 15 A each
- 120 or 230 V AC single-phase with earth group for the data system

Gas

- Ultra-high purity helium (99.999%) with less than 1 ppm each of water, oxygen, and total hydrocarbons
- High-purity nitrogen (99.5% pure, flow rate 15 L/min) gas supply for the API source and IRM

Dimensions (W x D x H)

- 1,270 x 805 x 703 mm (50 x 31.7 x 27.7 in.)

Weight

- 312 kg (678 lb) without data system, vacuum rough pumps, and optional items

Environment

- System averages 2,800 W (10,000 Btu/hr) output when considering air conditioning needs
- Operating environment must be 16–26 °C (59–78 °F) and relative humidity must be 50–80% with no condensation
- Optimum operating temperature is 18–21 °C (65–70 °F)

EASY-IC/ETD/PTCR ion source options

- Nitrogen supply for EASY-IC/ETD ion source options: Ultra-high purity nitrogen (UHP, 99.999%) with less than 1 ppm each water and oxygen

FAIMS Pro Duo interface option

- Nitrogen supply for FAIMS Pro Duo interface is 99.5% pure nitrogen at >20 L/min (100 psi)

 Learn more at thermofisher.com/TribriDApexBioPharma

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